"Ja

$\textbf{Neutrokine.} \alpha$

1	AAATTCAGGATAACTCTCCTGAGGGGTGAGCCAAGCCCTGCCATGTAGTGCACGCAGGAC	60
61	ATCAACAAACACAGATAACAGGAAATGATCCATTCCCTGTGGTCACTTATTCTAAAGGCC	120
121 1	CCAACCTTCAAAGTTCAAGTAGTGATATGGATGACTCCACAGAAAGGGAGCAGTCACGCC M D D S T E R E Q S R L	180 12
181 13	TTACTTCTTGCCTTAAGAAAAGAGAAGAAATGAAACTGAAGGAGTGTGTTTCCATCCTCC T S C L K K R E E M K L K E C V S I <u>L P</u> CD-I	240 32
241 33	CACGGAAGGAAAGCCCCTCTGTCCGATCCTCCAAAGACGGAAAGCTGCTGGCTG	300 52
301 53	TGCTGCTGGCACTGCTGTCTTGCTGCCTCACGGTGGTGTCTTTCTACCAGGTGGCCGCCC L L A L L S C C L T V V S F Y Q V A A L	360 72
361 73	TGCAAGGGGACCTGGCCAGCCTCCGGGCAGAGCTGCAGGGCCACCACGCGGAGAAGCTGC Q G D L A S L R A E L Q G H H A E K L P CD-II	420 92
421 93	CAGCAGGAGCAGGAGCCCCCAAGGCCGGCCTGGAGGAAGCTCCAGCTGTCACCGCGGGAC A G A G A P K A G L E E A P A V T · A G L CD-III	480 112
	TGAAAATCTTTGAACCACCAGCTCCAGGAGAAGGCAACTCCAGTCAGAACAGCAGAAATA K I F E P P A P G E G N S S Q N S R N K	-
541 133	AGCGTGCCGTTCAGGGTCCAGAAGAAACAGTCACTCAAGACTGCTTGCAACTGATTGCAG R A V Q G P E E T V T Q D C L Q L I A D CD-IV	600 152

FIG.1A

Neutrokine- α

601 153	ACAGTGAAACACCAACTATACAAAAAGGATCTTACACATTTGTTCCATGGCTTCTCAGCT S E T P T I Q K G S Y T F <u>V P W L L S F</u> CD-V	660 172
661 173	TTAAAAGGGGAAGTGCCCTAGAAGAAAAAGAGAAATATTGGTCAAAGAAACTGGTT K R G S A L E E K E N K I L V K E T G Y CD-VI	720 192
721 193	ACTTTTTATATATGGTCAGGTTTTATATACTGATAAGACCTACGCCATGGGACATCTAA FFIYGQVLYTDKTYAMGHLI CD-VII CD-VII	780 212
781 213	TTCAGAGGAAGAAGGTCCATGTCTTTGGGGATGAATTGAGTCTGGTGACTTTGTTTCGAT Q R K K V H V F G D E L S L V T L F R C CD-VII #	840 232
841 233	GTATTCAAAATATGCCTGAAACACTACCCAATAATTCCTGCTATTCAGCTGGCATTGCAA I Q N M P E T L P N N S C Y S A G I A K CD-VIII CD-IX	900 252
901 253	AACTGGAAGAAGGAGAACTCCAACTTGCAATACCAAGAGAAAATGCACAAATATCAC L E E G D E L Q L A I P R E N A Q I S L CD-X	960 272
961 273	TGGATGGAGATGTCACATTTTTTGGTGCATTGAAACTGCTGTGACCTACTTACACCATGT D G D V <u>T F F G A L K L</u> L CD-XI	1020 285
1021	CTGTAGCTATTTTCCTCCCTTTCTCTGTACCTCTAAGAAGAAAGA	1080
1081	CCAAAAAAAAAAAAAAA 1100	

FIG.1B

TNFalpha TNFbeta LTbeta FasLigand Neutrokine alpha	TNFalpha TNFbeta LTbeta FasLigand Neutrokine alpha	TNFalpha TNFbeta LTbeta FasLigand Neutrokine alpha
10 M S T E S M I R D V E L A E E A M T P P E R L M G A T P P E R L M Q Q P F N Y P Y P Q I Y W - V D S S A S S P W A P P G T V M D D S T E R E Q S R L T S C L K K R E E M K L K E C V S I M D D S T E R E Q S R L T S C L K K R E E M K L K E C V S I	40 50 60 60 60 60 60 60 60 60 60 60 60 60 60	70 80 90 90 90 90 90 90 90 90 90 90 90 90 90
	17 8 4 30 31 31	30 9 12 60 60 58

FIG.2A

TNFeripha TNFbeta LTbeta FasLigand Neutrokine al TNFbeta LTbeta FasLigand Neutrokine al Neutrokine al Neutrokine al FasLigand	Neutrokine alpha Neutrokine alphaSV
38 F L I V A G A T T L F C L L H F G V I G P Q R E F P-R 31 G A Q G L P G V G L	

FIG.2B

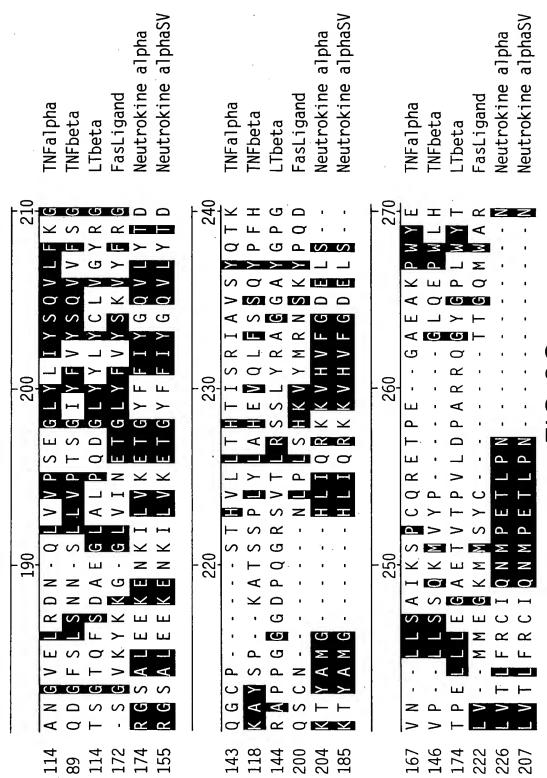


FIG.2C

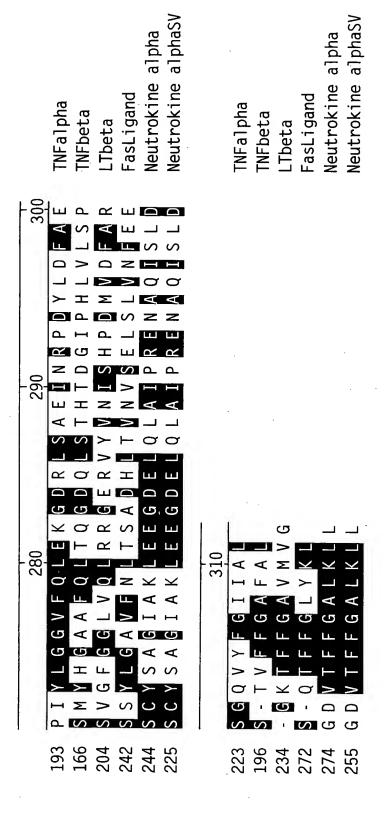
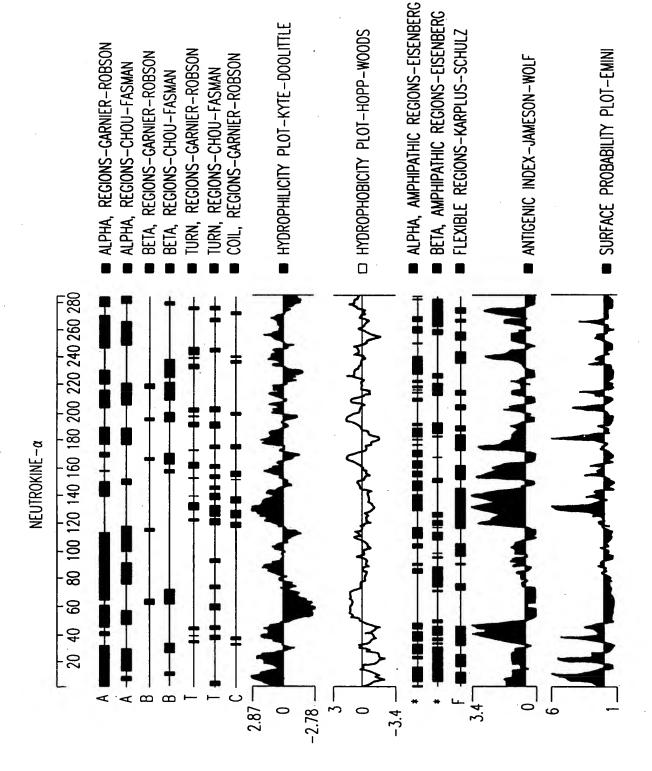


FIG.2D





1				50
701110440710	ariao, viadoo	adoo raa kaa	, ,	TateAccaca
51				100
dunc lunnan	TOTTUARCO	ACCAGCTCCA	GUAGAAGGCA	ACTOCAGTOA
101				150
GAACAGCAGA	AATAAGCGTG	CCGTTCAGGG	TCCAGAAGAA	ACAGICACIC
151				200
TATGGATGAC	TCCACAGAAA	GGGAGCAGTC	ACGCCTTACT	TCTTGCCTTA
AAGACTGCTT	GCAACTGNTT	GCAGACAGIG	AAACACCAAC	TATACAAAAA
201				250
GGCTCCCTTC	IGNIGCCACA	TTTGGGCCAA	GGAATGGAGA	GATTICTTCG
251				300
	CCCTCTNTCC	GATCCTCCAA	AGACGGAAAG	
GAAGGAAAGC	CCCTCTGTCC	GATCCTCCAA	AGACGGAAAG	CTGCTGGCTG
TCTGGAAACA	TTTTGCCAAA	CTCTTCAGAT	ACTCTTTNCT	CTCTGGGAAT
301				350
	GNTGGCATTG	TGTTCTTGCT	GNCTCAAGGT	
CAAAGGAAAA	TCTCTACTTA	GATTNACACA	TTTGTTCCCA	TGGGTNTCTT
351				400
	AATTCGGCAC AATTCGGCAC AATTCGGCAC S1 GTGCACGCAG GTGCACGCAG GTGCACGCAG ATACTGATAA GGACTGAAAA 101 CCTGTGGTCA CCTGTGGTCA CATGTCTTTG GAACAGCAGA 151 TATGGATGAC TATGGATGAC AAATATGCCT AAGACAGCAGA AGAAAAGAGA CAAAACTGCTT 201 AGAAAAGAGA CAAAACTGGN GGCTCCCTTC 251 GAAGGAAAAGC GAAGGAAAGC GAAGGAAAACC TCTGGAAACA 301 CAACCTTGNT CAACCTTGCT CATTGAAACT CAAAGGAAAA 351	AATTCA GGATAACTCTAAATTCA GGATAACTCTAATTCGGCA GAGCAAGGCC 51 GTGCACGCAG GACATCANCA GTGCACGCAG GACATCAACA ATACTGATAA GACCTACGCC GGACTGAAAA TCTTTGAACC 101 CCTGTGGTCA CTTATTCTAA CCTGTGGTCA CTTATTCTAA CATGTCTTTG GGGATGAATT GAACAGCAGA AATAAGCGTG 151 TATGGATGAC TCCACAGAAA TATGGATGAC TCCACAGAAA AAATATGCCT GCAACCTAC AAGACTGCTT GCAACCTAC AAGACAGGAAA AGAAATGAAA AGAAAAGAGA AGAAATGAAA CAAAACTGGN GGCTCCCTTC TGNTGCCACA 251 GAAGGAAAGC CCCTCTNTCC GAAGGAAACAC TCTGGAACA 301 CAACCTTGNT GNTGGCACT TCTGGAAACA TTTTGCCAAA 301 CAACCTTGCT GCTGGCACTG CATGAAACA TCTCTACTTA 351	A GGNTAACTCT CCTGAGGGGTAAATTCA GGATAACTCT CCTGAGGGGT .AATTCGGCA NAGNAAACTG GTTACTTTTT AATTCGGCAC GAGCAAGGCC GGCCTGGAGG 51 GTGCACGCAG GACATCANCA AACACANN GTGCACGCAG GACATCANCA AACACAGA ATACTGATAA GACCTACGCC ATGGGACATC GGACTGAAAA TCTTTGAACC ACCAGCTCCA 101 CCTGTGGTCA CTTATTCTAA AGGCCCCAAC CCTGTGGTCA CTTATTCTAA AGGCCCCAAC CATGTCTTTG GGGATGAATT GAGTCTGGTG GAACAGCAGA AATAAGCGTG CCGTTCAGGG 151 TATGGATGAC TCCACAGAAA GGGAGCAGTC TATGGATGAC TCCACAGAAA GGGAGCAGTC AAATATGCCT GAAACACTAC CCAATAATTC AAGACTGCTT GCAACTGNTT GCAGACAGTG 201 AGAAAAGAGA AGAAATGAAA CTGNAAGGAG AGAAAAGAGA AGAAATGAAA CTGNAAGGAG CAAAACTGGN AGGAAGGAGATGAAC GGCTCCCTTC TGNTGCCACA TTTTGGGCCAA 251 GAAGGAAAGC CCCTCTNTCC GATCCTCCAA GAAGGAAACA TTTTGCCACA TTTTGGGCCAA 251 GAAGGAAACA TTTTGCCAAA CTCTTCAGAT 301 CAACCTTGNT GNTGGCATTG TGTTCTTGCT CAACCTTGCT GCTGGCACTG CTGTCTTGCT CATGAAACA TTTTGCCAAA CTCTTCAGAT 301 CAACCTTGNT GNTGGCATTG TGTTCTTGCT CATGAAACT GCTGGCACTG CTGTCTTGCT CATTGAAACT GCTGGCACTG CTGTCTTGCT CATTGAAACT TCTCTACTTA GATTNACACA 351 TACCAGGTGG CCGCCCTGCA AGGGGACCTG CTNCCTNTTC TNTGGTAACC TCTTAGGAAG	A GGNTAACTCT CCTGAGGGGT GAGCCAAGCCAAATTCA GGATAACTCT CCTGAGGGGT GAGCCAAGCCAATTCGGCA NAGNAAACTG GTTACTTTTT TATATATGGT AATTCGGCAC GAGCAAGGCC GGCCTGGAGG AAGCTCCAGC GAGCAAGGCC GAGCAAGCC TATATATATGGT AATTCGGCAC GAGCAAGGCC GGCCTGGAGG AAGCTCCAGC GAGCACACACA AACACANN NNNCAGGAAA ATACTGATAA GACCTACACA AACACAGA TAACAGGAAA TAGTTCAGAG GACATCAACA AACACAGA TAACAGGAAA TAGTTCAGAG GACATCAACA AACACAGA TAACAGGAAA TAGTTCAGAG GACATCACA ACACACAC CTTCAAAGTT CATGTTCTTG GGGATGAATT GAGTCTGGT ACTTTGTTTC GAACAGCAGA AATAAGCGTG CCGTTCAGGG TCCAGAAGAA ATAAGCGTG CCGTTCAGGG TCCAGAAGAA AAACACCAAC AAATATGCCT GCAACTGNTT GCAGACAGTG ACGCCTTACT ACGCCTTACT ACGCACACAC CCAATAATTC CTGCTATTCAAACACCAAC CCAACACAC CTGNAAGGAG TGTGTTTCCA ACGCCTTACT ACGCCTTACT ACGCACACAC CTGAAACTGGA AGAAATGAAA CTGNAAGGAG TGTGTTTCCA ACGCCTTACT TGNTGCCACA TTTGGGCCAA TCCAACTTGC GAACACTAC GAACAGGAAAACTGAA AGAAATGAAA CTGAAGAGAA TCCCAACTTGC GATCCTCCAA AGACGGAAAG AGAAATGAAA CTTGAGAGA TGTTCCACATTCC CAACCTTGCT GAACACTAC CCTTCCAAA AGACGGAAAG TCCCAACTTGC CAACCTTGCT GATCCTCCAA AGACGGAAAG TCCCAACTTCC CAACCTTGCT GAACACTAC TCTTACAACA TCTTTACATTACA

HS0AD55R	401				450
HNEDU15X HSLAH84R HLTBM08R	GCAGGGCCAC ATAACCCAAA	CACGCGGAGA AAAANNTTAA	AGCTGCCAGC ANGGGTANGN	AGGAGCAGGA GNNANANGNG AGGTTTNTAT	GCCCCCAAGG GGGNNGTTNN
HSOAD55R	451				500
HNEDU15X HSLAH84R HLTBM08R	CCGGCCTGGA CNNGNNGNNT	GGAAGCTCCA TTTNGGNNTA	GCTGTCACCG TNTTNTNNTN	CGGGACTGAA GGGNNNNGTA NCNNTCTTTT	AATCTTTGAA AAAATGGGGC
USOADEED	501				550
HSOAD55R HNEDU15X HSLAH84R HLTBM08R	CNANGGGGGN	ттт	CAACTCCAGT	CAGAACAGCA	GAAATAAGCG
TIETDITOOK		••••••••		••••••	
HSOAD55R HNEDU15X	551 TGCCGTTCAG	GGTCCAGAAG	AAACAGTCAC	TCAAGACTGC	600 TTGCAACTGA
HSLAH84R HLTBM08R					
	601				650
HSOAD55R HNEDU15X HSLAH84R	TTGCAGACAG	TGAAACACCA	ACTATACAAA	AAGGATCTTA	CACATTTGTT
HLTBM08R				• • • • • • • • • • • • • • • • • • • •	
HSOAD55R	651				700
HNEDU15X HSLAH84R	CCATGGCTTC	TCAGCTTTAA	AAGGGGAAGT	GCCCTAGAAG	AAAAAGAGAA
HLTBM08R				• • • • • • • • • • • • • • • • • • • •	
HCOADEED	701				750
HSOAD55R HNEDU15X HSLAH84R		GTCAAAGAAA	CTGGTTACTT	TTTTATATAT	GGTCAGGTTT
HLTBM08R				• • • • • • • • • • • • • • • • • • • •	
HSOAD55R	751				800
HNEDU15X HSLAH84R	TATATACTGA		GCCATGGGAC	ATCTAATTCA	
HLTBM08R				• • • • • • • • • • • • • • • • • • • •	

LICOADEED	801				850
HSOAD55R HNEDU15X	GTCCATGTCT	TTGGGGATGA	ATTGAGTCTG	GTGACTTTGT	TTCGATGTAT
HSLAH84R HLTBM08R					
	851				900
HSOAD55R HNEDU15X	TCAAAATATG	CCTGAAACAC	TACCCAATAA	TTCCTGCTAT	TCAGCTGGCA
HSLAH84R HLTBM08R		••••••			
	901				950
HSOAD55R HNEDU15X	TTGCAAAACT	GGAAGAAGGA	GATGAACTCC	AACTTGCAAT	ACCAAGAGAA
HSLAH84R HLTBM08R		• • • • • • • • • • • • • • • • • • • •			
	951				1000
HSOAD55R HNEDU15X	AATGCACAAA	TATCACTGGA	TGGAGATGTC	ACATTTTTG	GTGCATTGAA
HSLAH84R HLTBM08R		• • • • • • • • • • • • • • • • • • • •			
	1001	·			1050
HSOAD55R HNEDU15X	ACTGCTGTGA	CCTACTTACA	CCATGTCTGT	AGCTATTTTC	CTCCCTTTCT
HSLAH84R HLTBM08R		• • • • • • • • • • • • • • • • • • • •		• • • • • • • • • • • • • • • • • • • •	• • • • • • • • • • • • • • • • • • • •
	1051				1100
	CTGTACCTCT		AATCTAACTG	AAAATACCAA	
HSLAH84R HLTBM08R		• • • • • • • • • • • • • • • • • • • •			
	1101				
HSOAD55R HNEDU15X	AAAAAA				
HSLAH84R HLTBM08R					

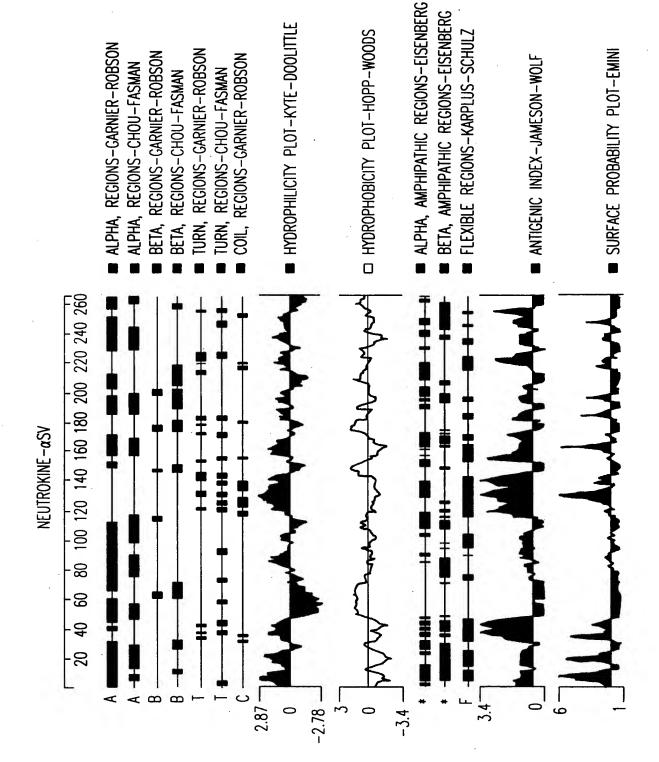
Neutrokine- αSV

1 1		A 60 20
61 21		A 120 _ 40
121 41		C 180 _ 60
181 61	CTCACGGTGGTCTTTCTACCAGGTGGCCGCCCTGCAAGGGGACCTGGCCAGCCTCCG L T V V S F Y Q V A A L Q G D L A S L R CD-II	G 240 _ 80
241 81		C 300 _ 100
301 101 C	GGCCTGGAGGAAGCTCCAGCTGTCACCGCGGGACTGAAAATCTTTGAACCACCAGCTCC G L E E A P A V T A G L K I F E P P A P CD-III #	A 360 120
361 121	GGAGAAGGCAACTCCAGTCAGAACAGCAGAAATAAGCGTGCCGTTCAGGGTCCAGAAGAGAGAG	A 420 140
121 141	ACAGGATCTTACACATTTGTTCCATGGCTTCTCAGCTTTAAAAGGGGAAGTGCCCTAGA T G S Y T F <u>V P W L L S F K R G S A L E</u> CD-IV	A 480 _ 160
481 161		T 540 _ 180
541 181	TTATATACTGATAAGACCTACGCCATGGGACATCTAATTCAGAGGAAGAAGGTCCATGT L Y T D K T Y A M G H L I Q R K K V H V CD-VI CD-VII	C 600 _ 200

Neutrokine- α SV

601 201 C	TTTGGGGATGAATTGAGTCTGGTGACTTTGTTTCGATGTATTCAAAATATGCCTGAAACA <u>F G D E L S L V T L F R C I Q N M P</u> E T D-VIII CD-VIII	660 220
661 221	CTACCCAATAATTCCTGCTATTCAGCTGGCATTGCAAAACTGGAAGAAGGAGATGAACTC L P N N <u>S C Y S A G</u> I A K <u>L E E G D E L</u> CD-IX CD-X	720 240
721 241	CAACTTGCAATACCAAGAGAAAATGCACAAATATCACTGGATGGA	780 260
781 261	GGTGCATTGAAACTGCTGTGACCTACTTACACCATGTCTGTAGCTATTTTCCTCCCTTTC G A L K L CD-XI	840 266
841	TCTGTACCTCTAAGAAGAAAGAATCTAACTGAAAATACCAAAAAAAA	900
901	AAA 903	

FIG.5B



 α > S ٩ S ш \leq 2 ۵. H S > ပ ш \checkmark __ \checkmark $\mathbf{\Sigma}$ ш ш α \leq \leq __ ပ S **—** \propto S Q ш α ш S Neutrokine-_ ∑ Alpha

41

S

Transmembrane Region

82 ш ⋖ \propto __ S V _ G O __ Ø Ø > O >-Щ. S > > ပ ပ S Ø Ø Þ __ \checkmark G \checkmark S

123 G ш G ۵. ⋖ ؎ ۵. ш ш \checkmark G Ø > × _ Þ ш ш G Ø \checkmark ۵. Ø G ⋖ G × ٩ \checkmark ш Ø 工 工 9 O

 \times Ω Σ SEQ A Q S Z 0. 0 ط April Ø TNF Η. ш ۵. G O > ⋖ ≃ \checkmark Z ∝ S Z O S

S

Z

200 170 139 $^{\circ}$ E O D F \leq 0 0 S $\mathbf{\omega}$ 9 \times \circ M A O Z ы o a s SEGA

8 1 SCC ∝ ш OF L 2 O D J & >> >= 5 > **—** \propto 工 O S ⋖ ۵. G > m

FIG. 7A-1

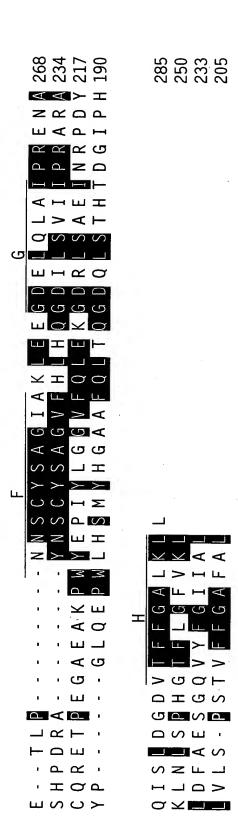


FIG.7A-2



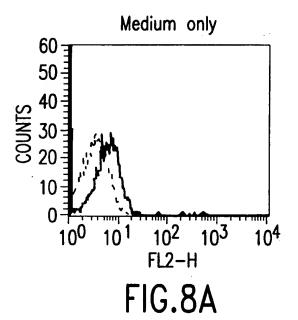
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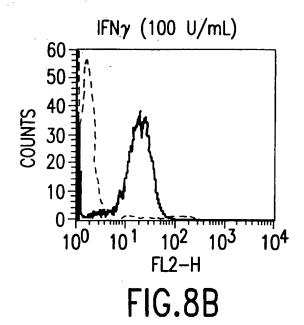
- 2.4 kb

Spleen
Lymph Node
Thymus
PBL
Bone Marrow
Fetal liver
Heart
Brain
Placenta
Lung
Liver
S. Muscle
Kidney
Pancreas

HL-60 HeLa K-562 MOLT-4 Raji SW480

FIG.7B





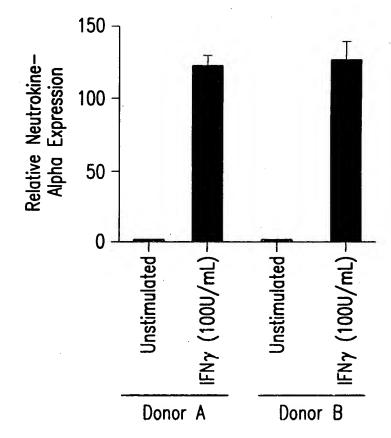
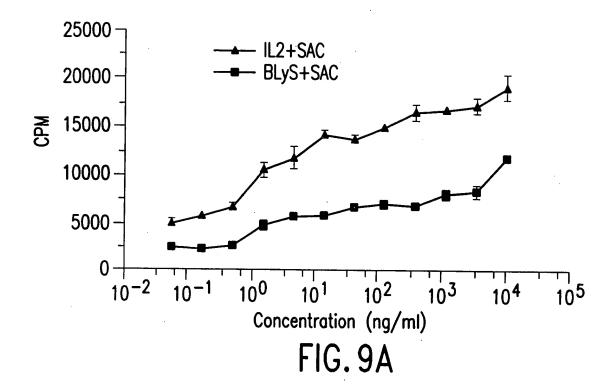
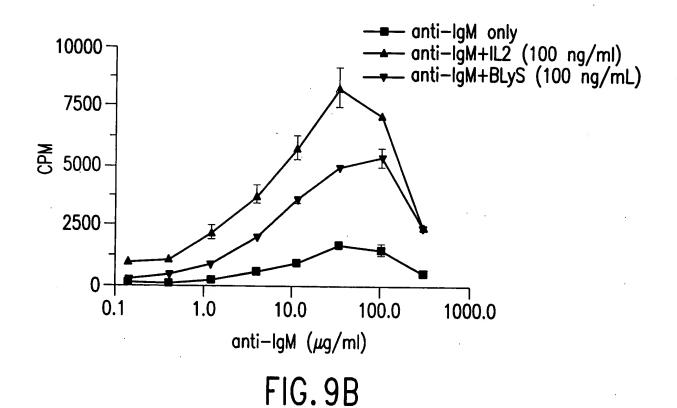
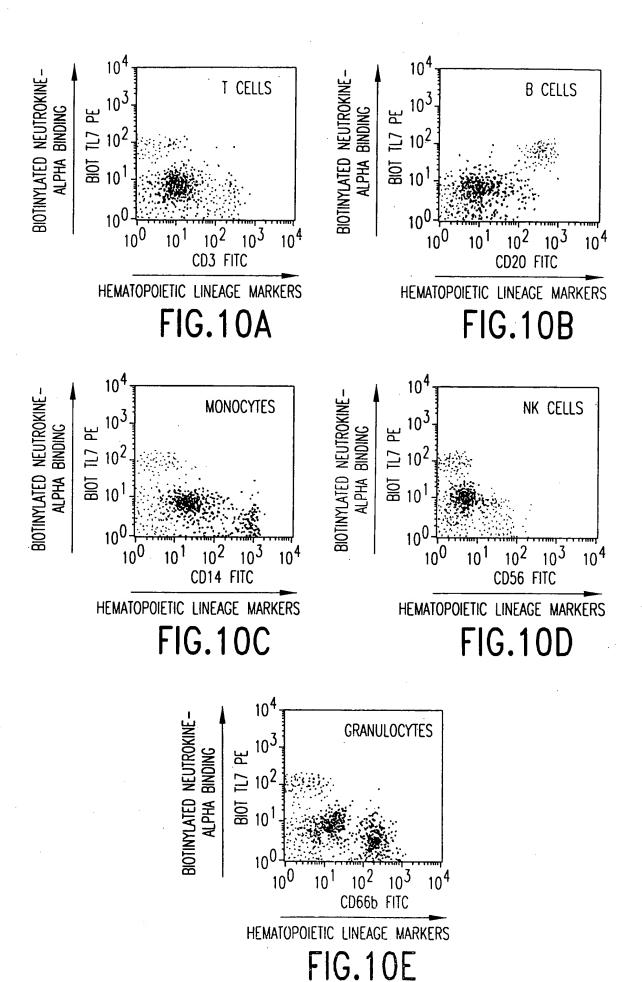
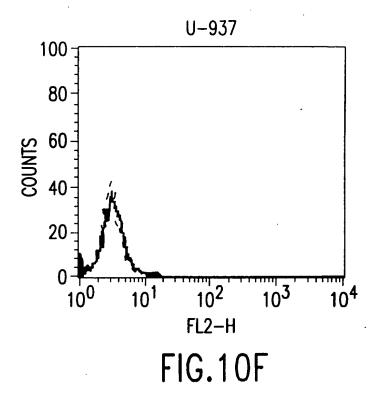


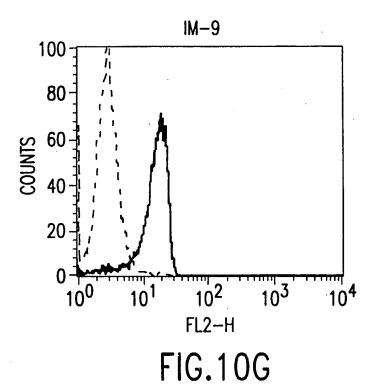
FIG.8C











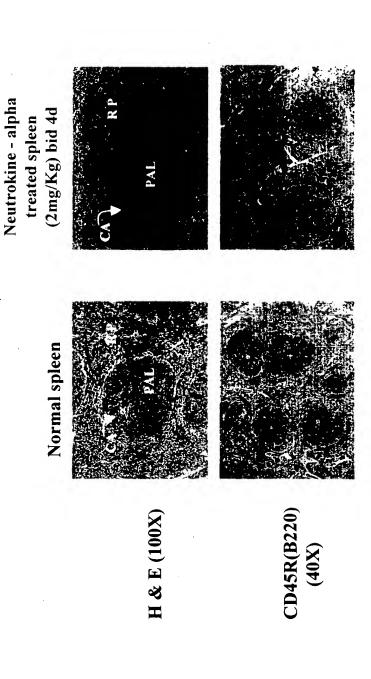


FIG.11A

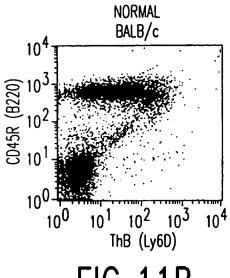


FIG. 11B

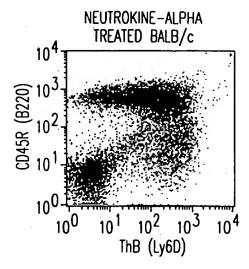


FIG. 11C

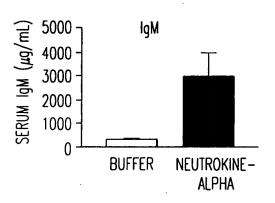


FIG. 11D

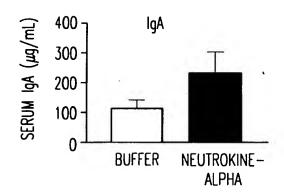


FIG. 11E

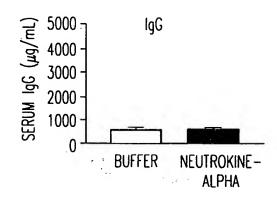


FIG. 11F

χ' \ γ' \